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ON LANDRY'S PARALYSIS, WITH THE REPORT OF A CASE.

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The literature of Landry's paralysis has become so extensive that it might be supposed that the pathology of the disease is thoroughly understood, but this is far from the truth. It is hoped that the report of the following case will add something of value to our knowledge of this subject.

H. W., a well-developed man of thirty-five years, a boilermaker, was admitted to the Philadelphia Hospital, November 26th, 1897. He denied having had syphilis, but acknowledged that he had been guilty of alcoholic excess and had had gonorrhœa.

For a month he had been feeling weak, but it was not until November 20th, 1897, that his symptoms became serious. At this time he complained of numbness in both hands, and of a slight inability to execute finer movements. He had stated previously that he had experienced numbness in both feet, but attributed this to the amount of walking he was obliged to do.

The next day, November 21st, while attempting to run for a street car, he fell, and was unable to rise without assistance. On November 22d, his legs gave way again while he was in a store, and he was unable to rise without help. On November 23d he was still able to walk on the street, but fell, and could not rise until he was picked up and assisted to his home. During November 23d and 24th the loss of power gradually increased, more markedly at first in the upper limbs, until by

November 25th he was completely paralyzed in all the extremities. He began at this time to have considerable difficulty in breathing, and also had a cough. This was his condition when he was admitted to the Philadelphia Hospital, to the service of Dr. Mills, November 26th.

When he was examined, November 27th, he was perfectly conscious, and gave intelligently a full history of his illness, but he suffered from intense dyspnœa. He spoke slowly and distinctly. He was able to move the pelvis up and down to a slight extent, and to rotate the lower limbs a little at the hip joints, but otherwise he was completely paralyzed in all four extremities. The tendon reflexes in the lower limbs were entirely lost, and in the upper the response to a tap over the biceps muscles was feeble and soon exhausted. The limbs were slightly rigid. The dysphagia was great, and he choked in drinking. The sphincters were not affected. Numerous râles were heard in the lungs. The expansion of the chest was good on both sides. The percussion revealed nothing abnormal. The pulse was rapid, but forcible. The apex beat of the heart was in the fifth interspace and was strong. No cardiac murmurs were detected.

Sensation for heat, cold, pain and touch was normal everywhere. He had complained at first of some pain in the posterior part of both thighs, and especially behind the knees. Pain had passed away at the time of examination, except in the posterior part of the cervical region, especially when the head was not supported. No tenderness was present in the back of the neck on pressure, or over any of the nerve trunks of the body or limbs, except in a small area on the right side, under the outer third of the clavicle.

The ocular muscles were not paralyzed, and the pupils responded to light and in accommodation. The ophthalmoscopic examination revealed nothing abnormal.

The patient stated that he had noticed swelling of the face in the morning, especially under the eyes, for some time. The color of the urine was reddish; its reaction was acid; its specific gravity was 1024, and it contained a little sediment, in which bladder cells and leucocytes were found, but neither albumin nor sugar was present.

The man became gradually worse, and he died November 27th, 1897.

The notes of the necropsy, made twenty-four hours after death, by Dr. William B. Jameson, are as follows:

The heart contained fluid blood and some clots; its valves were normal, and its weight was 400 grammes. At the left apex of the lung, and along its posterior surface, were extensive pleural adhesions. The left lung was markedly emphysematous, and showed extensive catarrhal pneumonia in the lower lobe. Its weight was 1,100 grammes. The right lung showed minute patches of catarrhal pneumonia throughout. It was also emphysematous, but less so than the left. Its weight was 1,250 grammes. Some purulent excretion was noted in the bronchi of both lungs. The spleen was normal. The left kidney was distinctly red in color, and the capsule stripped easily, leaving a smooth surface. The cortex was normal in depth, and the vessels were not notably thickened. No gross lesions were observed. The weight was 180 grammes. The right kidney presented the same appearance as the left, and its weight was 190 grammes. The surface of the liver was smooth. The capsule was not thickened. Considerable hypostatic congestion and numerous, but not extensive, areas of fatty infiltration were observed. Its weight was 2,270 grammes. The meninges of the cord were normal, and no gross lesions were observed in the cord or brain. The cord appeared to be hyperæmic. The pia matter was deeply injected. The weight of the brain was 1,450 grammes.

The gross examination, therefore, showed chronic pleurisy of the left side, bilateral catarrhal pneumonia, pericardial effusion (about two ounces of clear serum), emphysema and hyperæmia of the gray matter of the cord, pons and oblongata.

One of the external popliteal nerves was examined by the method of "teasing" and staining with a one per cent. solution of osmic acid. Many of the medullary sheaths were greatly swollen, and in some fibres the myelin was entirely broken up into black balls. The nuclei were also more numerous. Many of the fibres appeared normal, or only slightly altered, and the process had evidently been of too short duration to cause involvement of all the fibres.

In one of the cutaneous nerves removed from the sole of the foot the lesions were less intense. The carmine stain showed many small axis cylinders in the external popliteal nerve, and occasionally one or more axis cylinders somewhat swollen.

The cells of the ventral horns throughout the cord were tumefied and more or less rounded; their centres were more homogeneous than normal, and contained scattered granules stained purple with the thionin after Lenhossék's method; the nucleus was displaced to the periphery of the cell, but hernia of the cell was not observed. The nucleolus stained an intense purple, and contained often one, two or three vacuoles, which are recognized as existing in normal nucleoli. At the periphery of the cells the chromophilic elements were still preserved, and the dendrites were intact. The destruction began in the chromophilic elements situated about the nucleus. and evidently had not involved all the cellular contents. Some of the cells of the ventral horns were normal, which we should expect, in view of the fact that many nerve fibres were preserved. The carmine stain, as well as the Nissl stain, showed the tumefaction of the cells and the displacement of the nucleus.

The cells in the sacral region were as much affected as those elsewhere in the cord, notwithstanding the absence of vesical and rectal symptoms. The cells of the column of Clarke appeared to be normal.

The medullary sheaths in the anterior and posterior roots were stained black by Marchi's method, and this was noticed especially in the extramedullary portion. A slight cellular infiltration was seen within the roots, meninges and cord in some of the sections.

In the thoracic segments, in which more roots were obtained than in sections from other parts of the cord, the posterior roots presented a number of swollen axis cylinders when the carmine was employed as a stain; a few swollen ones were also found in the anterior roots, but they were not as numerous and not as large as those in the posterior roots.

Sections from the cervical, midthoracic and lumbar regions stained by the method of Marchi revealed numerous black dots scattered all over the transverse area of the cord, but these are hardly to be considered as indicative of degeneration. We have seen sections from presumably normal spinal cords stained by this method in which these same diffuse black masses were present in moderate amount. The swelling of the axis cylinders in the spinal roots, as seen by the carmine stain, renders the pathological nature probable of some at least of these black dots in the roots.

Some of the cells of the twelfth and of the motor fifth and tenth nuclei stained diffusely, but this may have been due largely to postmortem changes, for the nuclei within these cells were not displaced.

One or two prominent accumulations of round cells were found within the oblongata, but not elsewhere.

The cerebral cortex appeared to be intact, and the giant cells of the paracentral lobule were normal.

No hæmorrhages were observed anywhere within the central nervous system.

No microörganisms could be found, either by the thionin stain or by Gram's method, and cultures made from the spinal cord, and examined by Dr. Samuel S. Kneass, yielded negative results.

We understand by Landry's paralysis a disease in which the rapid loss of motor power usually begins in the lower limbs, and the paralysis is flaccid and associated with paræsthesia and loss of the tendon reflexes. The upper extremities are soon involved, and bulbar symptoms develop after a few days. Pain is not a prominent symptom. Death occurs within a week or ten days, though in some cases it may be delayed, and in others more rare recovery may ensue. There may be a descending, as well as an ascending form of paralysis. The electrical reactions are normal, and the patients are perfectly conscious of their condition.

This may be considered quite a characteristic picture of Landry's paralysis, but the lines cannot always be sharply drawn, either clinically or histologically. Thus Oppenheim[1] says that spontaneous pain is exceptional, acknowledging thereby that it may occur. He likewise says that in some cases reaction of degeneration and vesical and rectal symptoms are noted. Muscular degeneration has also been observed.

It is evident that the distinction between Landry's paralysis and polyneuritis cannot be sharply made if Oppenheim's views are accepted, and this is especially true if we follow the teaching of Nauwerck and Barth.[2]

Goldflam reports a case of Landry's paralysis which for a time he regarded as one of paroxysmal paralysis.[3]

Raymond,[4] after an excellent presentation of the subject of acute ascending paralysis, says that the disease may ascend or descend, may begin or end with bulbar symptoms, and the electrical reactions may be altered. Disturbance of sensation may be absent, slightly pronounced, or very marked. Paræsthesia, pain, hyperæsthesia, or anæsthesia may be present. The tendon reflexes may be preserved or abolished.

Bailey and Ewing[5] have tabulated a large number of cases of Landry's paralysis, and much labor will be spared future writers on this subject. They state that the nerves were examined in osmic acid only in two of the sixteen cases without lesions, and in none of these cases were the most improved methods for staining the cells employed. It matters little how skilled an investigator may be, he will be unable to detect very early cellular changes by the carmine stain, or early nerve lesions by the hæmatoxylin stain of Weigert. The most reliable method for the determination of beginning alteration in nerve fibres is the method of "teasing" and staining the tissue in the fresh state with osmic acid.

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[1] Oppenheim: Lehrbuch der Nervenkrankheiten, p. 357.

[2] Nauwerck and Barth: Ziegler's Beiträge, vol. v.

[3] Goldflam: Deutsche Zeitschrift f. Nervenheilkunde, vol. xi., Nos. 3. 4.

[4] Raymond: Leçons sur les Maladies du Système Nerveux, Deuxième Série.

[5] Bailey and Ewing: The New York Medical Jour., 1896, No. 2.

Bailey and Ewing state that in nine of the fourteen cases in which changes were found in the cord alone, the nerves were not examined, and in only one of these nine cases were the clinical symptoms of neuritis present. This latter statement is of limited value. It is the experience of every oculist that optic neuritis may be present and cause little functional disturbance, or that impairment of sight may be noticed with clear media and apparently normal fundus. Organic changes in the body may be latent for some time. The symptoms of neuritis may be chiefly those of involvement of motor fibres, as in this case we report.

Bailey and Ewing believe that the remaining five cases conclusively demonstrate that a lesion limited to the cerebrospinal axis may produce acute ascending paralysis. These five cases, we take it, are those of Eisenlohr, Hoffmann, Immermann, Hlava, and Œttinger and Marinesco. Unless the nerves were examined by osmic acid, these cases are not conclusive of the exclusively spinal origin of Landry's paralysis.

In regard to Eisenlohr's[6] case, we find the statement that transverse sections of the anterior roots from different parts of the cervical region, stained with carmine, presented normal fibres. We find no mention of a careful examination of the peripheral nerves. This case, therefore, is not conclusive.

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[6] Eisenlohr: Virchow's Archiv, vol. lxxiii., p. 73.

In Hoffmann's[7] case pathological changes were only found in the facial nerve; all the other nerves examined were normal. The intramedullary portions of the anterior roots were much altered. The nerves had been hardened in Müller's fluid, and do not seem to have been examined in the fresh state. We are sure that early lesions of nerve fibres may be overlooked in preparations hardened in Müller's fluid.

In regard to Immermann's[8] case, the muscles and peripheral nerves were intact. No mention is made of the method of examination of the nerves. Immermann says that the case shows that there is a form of acute anterior poliomyelitis which clinically corresponds to Landry's paralysis.

In regard to Hlava's[9] case, the sciatic and ulnar nerves were examined, and while mast cells were found in both, no degeneration was detected. Unfortunately no mention of the method of examination of the nerves is given in this abstract, and the original paper is not accessible to us.

In Œttinger and Marinesco's[10] case the alterations in the central nervous system were great, without appreciable lesions in the peripheral nerves.

Of the six cases of acute anterior poliomyelitis which Bailey and Ewing would include as cases of Landry's paralysis, they state that four show an involvement of the cord alone. In the abstract of Rissler's[11] cases we find that secondary degeneration of motor nerves was observed in the acute cases, and that in the more chronic ones the roots were diminished in size.

In Redlich's case degeneration was noted in the brachial plexus.

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[7] Hoffmann: Archiv f. Psychiatrie, vol. xv., 1884.
[8] Immermann: Neurologisches Centralblatt, 1885, p. 304.
[9] Hlava: Schmidt's Jahrbücher, 1891, 232, p. 244.
[10] Œttinger and Marinesco: Semaine Médicale, 1895, p. 45.
[11] Rissler: Neurologisches Centralblatt, 1889, p. 422.

In Goldscheider's the nerves were not examined.

In Dauber's[21] case of poliomyelitis it is distinctly stated that the anterior roots were pathologically altered.

In regard to the cases collected by Bailey and Ewing, in which the peripheral nerves alone were affected, these writers state that only one case shows that a lesion limited to the peripheral nerves may cause typical symptoms of fatal acute ascending paralysis. This is evidently Dejerine's case, which was examined before Nissl's stain was in vogue.

In Eisenlohr's[18] case (Case I) the central nervous system was put in Müller's fluid, and Nissl's stain was probably not employed.

A total of twenty-eight recorded cases of Landry's paralysis in which lesions were found, as collected by these writers, must make us somewhat sceptical toward the report of those cases in which no lesions were noted. Only in a few cases have bacteria actually been observed.

In the case of Landry's paralysis reported by Bailey and Ewing (l. c.) intense perivascular cellular infiltration was found within the cord, which we have not noticed in our case, except in one or two regions of the oblongata.

The changes which they found in the motor cells are not unlike those described by us. The peripheral nerves were not examined by them, which is much to be regretted. The fact that the nerve roots in the upper thoracic and cervical segments were intact, especially as considerable cellular infiltration was seen within them, does not exclude the possibility of peripheral degeneration. It is very true that, if such degeneration had been present, it might have been secondary to the cord lesions; but it might also have occurred at the same time as the spinal lesions. A toxin may affect the most distal portion of the peripheral neuron simultaneously with its attack on the cord. We question the possibility of deciding from the nature of the cellular lesions whether the change is primarily within the cell or in the terminal ramifications of the neuron.

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[21] Dauber: Deutsche Zeitschr. f. Nervenheilk., vol. iv.

[18] Eisenlohr: Deutsche med. Wochenschrift, No. 38, 1890.

In Hun's[14] case, which, clinically, was quite a typical one of Landry's paralysis, a slight cerebral and spinal meningitis of quite recent origin, a degeneration of some of the fibres of the anterior roots of the cauda equina, and a thickening and infiltration of the walls of the anterior spinal vein were noted. Some portions of the cord were hardened in alcohol, but no detailed statements are given of the condition of the motor cells as examined by Nissl's stain. No changes were found in the peripheral nerves by osmic acid.

In this case the moderate infiltration of the spinal pia and its vessels with small round cells might be regarded as the early stages of meningitis, and, had the patient lived longer, it is possible that meningitic pains would have been experienced. We may thus understand how easily sensory symptoms are added to the purely motor ones of Landry's paralysis.

Hun believes that his case goes far to prove that acute ascending paralysis may exist without any appreciable lesion. In view of this statement, we cannot help reregretting that more exact information of the condition of the cells, as stained by Nissl's method, could not be given.

Dejerine[15] states that certain toxins cause paralysis without neuritis histologically appreciable, and from the text it is evident he has not in mind myelitis as the cause of such paralysis. He refers to the experiments of Charrin as a proof of his statement. Babinski and Charrin[16] produced motor paralysis in rabbits by the injection of the bacillus pyocyaneus, or merely the soluble products of this microörganism obtained by cultures. They examined the muscles, nerves and central nervous system of these animals at different periods of the paralysis, even after two months had elapsed, and employed various methods, but their results were absolutely negative. These experiments show us that we may expect negative findings in some cases of Landry's paralysis.

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[14] Hun: The New York Medical Journal, vol. liii., p. 609.

[15] Dejerine: La Médecine Moderne, Dec. 21, 1895.

[16] Babinski and Charrin: Comptes rendus de la Société de Biologie, 1888, p. 257.

Hun (l. c.) states that in every reported case of Landry's paralysis due to neuritis few or no symptoms of bulbar paralysis were observed, and that these cases also presented decided disturbance of sensibility, manifested by severe pain or by extensive anæsthesia, or paralysis of the sphincters, or atrophy of the muscles, with more or less well-marked electrical reaction of degeneration, and tenderness on pressure.

In our case, in which polyneuritis was certainly present, although equally marked changes were found in the cell bodies within the cord, bulbar symptoms were manifested in great dyspnœa and dysphagia. No disturbances of objective sensation were present, and only slight pain, if we include the pain experienced for a short time and limited to one or two regions. Paræsthesia was noted, but no involvement of the sphincters, no muscular atrophy, and no tenderness on pressure, except in one very limited area. Unfortunately the electrical reactions were not taken. This absence of tenderness of the muscles on pressure is interesting, as a number of writers state that even in the motor form of neuritis in which sensation is apparently normal, pressure of the affected muscles usually causes pain.

The case reported by Ballet and Dutil[17] may possibly be regarded as representing a later stage of a condition similar to that in Hun's case. Sensation in all its forms was intact. The spinal vessels, especially those in the anterior horns, were enormously dilated, and considerable leucocytic infiltration was found. The cells of the posterior horns, those of the columns of Clarke, and especially those of the anterior horns, presented destruction of the chromophilic elements, cloudiness of the cell protoplasm, destruction or rupture of the cellular processes, and nuclear changes. It was, therefore, a case of diffuse myelitis. The roots and peripheral nerves showed an early stage of degeneration. No microbes could be found.

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[17] Ballet and Dutil: Bulletins et Mémoires de la Société Médicale des Hopitaux de Paris, 1895, p. 684.

The case reported by Marie and Marinesco[18] also shows that ascending paralysis, especially in the wider acceptation of the term, may be due to disease of the central nervous system, although Nauwerck and Barth stated, at the time they wrote their paper, that the proof of such an origin of the disease had not been given.

This case reported by Marie and Marinesco was quite a typical one of Landry's paralysis, except that the patient suffered intense pain in the entire body. Objective sensation was diminished only for a time. Intense mononuclear leucocytic infiltration was observed in the anterior horns as well as infiltration of a less intense degree in the posterior. Some of the ganglion cells of the anterior horns were swollen and the chromophilic elements had disappeared. Some of the processes and cell bodies were divided. In the cervical region where the disease was not so far advanced, it was easy to see that the elements nearest the nucleus had disappeared, while those at the periphery of the cell were preserved. The nucleus was displaced. The peripheral nerves seemed to be intact.

We have mentioned this case somewhat in detail on account of its importance. It presents cellular changes from myelitis, some of which are very much like those seen when the axis cylinder is cut, and it shows the difficulty in deciding as to the primary or secondary nature of the cellular changes. It proves that the peripheral nerves are not always diseased when the cell body is much altered;

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[18] Marie and Marinesco: Bulletins et Mémoires de la Société Médicale des Hopitaux de Paris, 1895, p. 659.

and it shows, finally, that Landry's paralysis may be due to purely central lesions.

The central form of Landry's paralysis, according to Bruns,[19] is chiefly in the area of the cord nourished by the central arteries. This central form of Landry's paralysis, like the acute anterior poliomyelitis, may be due to a poison which gains entrance to the cord chiefly through the anterior spinal arteries, which we know nourish the gray matter. It is not necessary that the bacteria themselves should be found within the cord, as numerous experiments have shown that the toxins alone are sufficient to produce such changes. Ballet,[20] Phisalix and Charrin,[21] refer to a number of these investigations.

The case reported by Œttinger and Marinesco[22] was due to central lesions also, and the peripheral nerves did not present any appreciable alteration. Sensation for touch, pain and temperature was much diminished. Bacteria were numerous within the cord. Marie in discussing this case (l. c.) says that certain authors have been wrong in stating that acute ascending paralysis is due to peripheral neuritis, but, "in reality, it is due, purely and simply, to lesions of the nervous centres." Our case would hardly support this statement.

The close connection of Landry's paralysis and typical polyneuritis may be seen in a case reported by Raymond.[23] The paralysis was not of the ascending type, but he states that no clinician would have hesitated at first to call the case one of Landry's paralysis, although the later developments of the case made this diagnosis untenable. The muscles and nerves of the lower extremities became very painful on pressure, the muscles of the extremities atrophied, and presented the reaction of degeneration.

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[19] Bruns: Allgemeine Zeitschrift für Psychiatrie, vol. liii.

[20] Ballet: Psychoses et Affections Nerveuses.

[21] Phisalix and Charrin: Comptes rendus de la Société de Biologie, No. 3, 1898.

[22] Œttinger and Marinesco: Bulletins et Mémoires de la Société Médicale des Hopitaux de Paris, 1895, p. 63.

[23] Raymond: Leçons sur les Maladies du Système Nerveux, Deuxième Série.

The changes which occur within a nerve in parenchymatous inflammation are like those of descending degeneration and, notwithstanding the many causes of peripheral neuritis, the lesions of most forms are similar, though possibly the perfection of our methods of examination may reveal a variety of histological forms. The changes in a nerve undergoing degeneration consist of multiplication of the nuclei of the sheath of Schwann, increase in the amount of protoplasm within the fibre, destruction of the myelin with the formation of balls of various sizes, and destruction of the axis cylinder. When the neuritis is due to traumatism, the inflammation is said to be chiefly in the connective tissues and vessels of the nerves, and the parenchyma is only secondarily affected.

Babinski voices the opinion of many neuropathologists when he says that in peripheral neuritis—as distinguished from central or secondary neuritis in which the nerves are altered secondarily to lesions within the spinal cord—the nerves are only altered at their periphery, and their trophic centres appear perfectly normal, or, at least, are only slightly altered.

It is exceedingly difficult when the neuritis is supposed to be due to a toxic or infectious agent, to decide whether the cell of origin is altered primarily or secondarily. Experimentally it has been shown that very decided changes occur within the cell when its fibre has been cut (J. Babinski,[24] p. 662). Ballet[25] discusses the subject quite fully. He says périphéristes believe that the nerve may be altered independently of the cell body, i. e., the peripheral part of the neuron is to a certain extent more susceptible to morbid processes than the corpus. He cites as supporters of this view Leyden, Dejerine, Pitres and

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[24] Babinski: Traité de Médecine, vol. vi.

[25] Ballet: Psychoses et Affections Nerveuses.

Vaillard, and Strümpell. These authors support their opinion on the fact that more or less pronounced lesions of the peripheral nerves may be found with few changes in the roots, and none in the cord.

The centralistes, on the other hand, believe that the cell is also involved, though perhaps only functionally. Among these may be mentioned Erb, Remak, Eisenlohr, Charcot, Brissaud, Babinski and Marie. These base their opinion on the bilaterality and symmetry of the nerve lesions; on the topography of the sensory or motor disturbances which does not always correspond to the distribution of the nerve trunks, as seen, for example, in the escape of the supinator longus muscle in lead palsy; and on the degenerative rather than the inflammatory character of the nerve lesions (Erb). Babinski and Ballet state that it is quite possible to have a truly inflammatory neuritis localized to a limited area, and that the changes within the nerve below this point are of a degenerative character.

Ballet (l. c. page 359) reports a case which shows in some of the features a resemblance to Landry's paralysis, though of long duration. A man became weak in the lower limbs from unknown cause, and had numbness and tingling. Within a few weeks the weakness became paralysis and atrophy was noticed. The upper limbs also became involved, and reaction of degeneration was noted. With the exception of numbness and tingling the sensation was normal. The tendon reflexes were absent, and the sphincters were intact. The peripheral nerves were found much degenerated, and the anterior roots were only slightly affected. In the anterior horns of the cord the cells were less numerous than normal; they were swollen, and the nucleus was displaced toward the periphery. The symptoms had lasted eight months.

The cellular changes which Ballet found in this case (l. c., p. 365) were very much like those we describe. He speaks of the destruction of the chromophilic elements, at first of those about the nucleus, and finally of all within the cell; and of displacement and change of form and more intense staining of the nucleus. The vessels and neuroglia of the cord were normal.

Ballet (l. c.) after referring to the experimental work of Nissl, B. Onufrowicz, and Marinesco, reports cellular changes very similar to those in his case of neuritis; changes which were found by Dutil in guinea pigs after section of the sciatic nerve. Only in one of the three animals was degeneration of the central end of the cut nerve found, and this animal was killed thirty-seven days after the operation. Some of the cells of the anterior horn had disappeared. This degeneration of the central end of the cut nerve was not found when the guinea pigs were killed six days or seventeen days after the operation. Ballet believes that this degeneration was secondary to the cellular changes, and was not an ascending degeneration. He states that the cases of neuritis in which the cells of origin within the cord have been found normal have not been studied by Nissl's method, though in some cases the neuritis may not be sufficiently intense to cause cellular alteration.

Marinesco also has explained the so-called ascending degeneration of the central end of a cut nerve on the supposition that it is secondary to changes within the cell body, and is really of the nature of Wallerian degeneration.

Marinesco says that Œttinger, Korsakoff, Köpper, Schaffer, Erlitzky, Achard and Soupault have described lesions of the cells of the anterior horns in alcoholic paralysis; Dejerine and Œrtel in diphtheria; Oppenheim, Popoff, Rosenbach in lead palsy; and that Fuchs, Goldscheider and Moxter, Giese and Pagenstecher, Ballet and Dutil have found these cellular changes in polyneuritis. Much evidence, therefore, is in favor of the view that poisons have a very decided effect on the motor cells of the anterior horns.

Marinesco[26] describes a case of polyneuritis in which the nerves were found greatly altered; the anterior and posterior roots seemed to be intact, but changes were found within the cell body very much like those in the case we report. He speaks of a resemblance of these cellular changes to those which occur when a nerve is cut, and states that he is the first to call attention to this. Figure 17 of his paper would represent very well one of the cells of the anterior horns in our own case. He calls attention to the fact that Strümpell and Raymond have believed that a toxic agent may act at the same time on the nervous centres and on the peripheral nerves. He believes that he can make a distinction between the secondary changes in a nerve cell, as seen when its fibre is cut, and primary changes, such as occur after compression of the abdominal aorta. In the latter the destruction of the chromophilic elements begins at the periphery of the cell, the perinuclear layer is intact, and the nucleus is central, while in later stages the trophoplasm (the achromatic portion) of the cell presents large spaces resulting from its partial destruction.

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[26] Marinesco: Revue Neurologique, 1896, p. 129.

Marinesco regards this degeneration of the trophoplasm as an early lesion in all acute primary affections of the spinal cord, and has observed it in two cases of Landry's paralysis. Whenever the trophoplasm is altered, the lesion is irreparable, for there is no regeneration of nerve cells as shown by the work of Stroebe.[27]

The question, therefore, as to the primary or secondary involvement of the cell of origin of the peripheral neuron is one of some importance. Restoration of function is not uncommonly noted when the lesion begins in the axis cylinder and the cell is altered secondarily, but according to Dejerine,[28] not a single case of diffuse myelitis or of poliomyelitis with restoration ad integrum has been reported.

Disease of the cell of origin of the motor nerve fibre has been found by other investigators in neuritis. Dejerine and Theohari[29] have found it in neuritis of the seventh nerve, and Soukhanoff[30] recently in polyneuritis. Other cases are on record.

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[27] Stroebe: Centralblatt f. allgemeine Pathologie und pathologische Anatomie, vol. vi., 1895.

[28] Dejerine: La Médecine Moderne, Dec. 21, 1895.

Schaffer[31] has studied the cells in the anterior horns in several cases of tabes in which trophic lesions were observed, and has found that the cellular changes are the same whether there is amyotrophy, osteopathy or arthropathy. In the early stages the chromophilic elements about the nucleus are broken up into granules, and only when the cell body is affected, in toto, are the nucleus and nucleolus altered. The dendrites are involved later than the cell body, and may be found relatively intact when the cell body is seriously altered. The partially degenerated cells are more numerous than the totally degenerated. Schaffer concludes from his studies of cellular lesions from toxic, infectious and trophic causes, as well as from direct disturbance of nutrition, that the Nissl stain does not show specific changes in any case, and that in every form of cellular disease the lesion is chromatolysis, which in its essential features is always the same. This chromatolysis Schaffer does not regard as a lésion banale in the sense used by Dejerine and Thomas, but looks upon it as an index of the cell's vitality.

Mourek and Hess,[32] after performing a number of experiments in poisoning rabbits, concluded that in all the cases the chromatolysis was the same, and that the Nissl elements presented no characteristic alterations for the different poisons. The investigations of Van Gieson,[33] and more recently those of Ewing, show us that the importance of chromatolysis is not held to be equally great by all histologists.

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[29] Dejerine and Theohari: Comptes rendus de la Société de Biologie, Dec. 4, 1897.

[30] Soukhanoff: Abstract in Revue Neurologique, No. 2, 1898.

[31] Schaffer: Monatsschrift f. Psychiatrie und Neurologie, vol. iii., No. 1.

[32] Mourek and Hess: Revue Neurologique, 1897, p. 667.

[33] Van Gieson: Medical Record, April 9, 1898, p. 526. Ewing: Idem.

The early changes which Schaffer has found in the spinal cells of tabetic patients are about the same as those observed by us in the case of Landry's paralysis, and like those noted in cases reported as polyneuritis. Schaffer believes that the tabetic changes are primarily in the cell body, but we must confess that we are not convinced of the correctness of this view, and it is possible that such cellular alterations in tabes are secondary to neuritis. In this sense Dejerine[34] would still be right in that he believes the muscular atrophy of tabes is due to neuritis. Schaffer found that normal cells were mingled with diseased ones. This could be explained by the fact that usually in neuritis some of the nerve fibres are intact, and secondary changes in the cells are only found in those belonging to the altered fibres; it could, however, be used to explain the partial involvement of nerve fibres if the cellular changes are regarded as primary. Schaffer believes that the partial degeneration of a nerve cell causes degeneration at the periphery of the neuron, in the terminal ramifications of the fibre, and as the cellular changes increase the degeneration of the fibre creeps upward. May it not be equally true that the lesion is primarily in the nerve termination, or simultaneously in the nerve termination and in the cell body? May it not be true that the peripheral lesion leads to partial degeneration of the cell body? It may be that the portion of the neuron furthest from the nucleus, as Erb and Strümpell believe, is the portion most susceptible to toxic agents. We acknowledge the force of all that Schaffer says, but we cannot regard his arguments as final. It seems to us that the question as to the primary or secondary involvement of the motor cells in tabes and polyneuritis is still open.

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[34] Dejerine: Sur l'Atrophie Musculaire des Ataxiques.

Berger[35] has found the cells of the anterior horns much degenerated in cases of dementia paralytica, and among other changes he describes conditions very similar to those seen by us in our case of Landry's paralysis. He ascribes the muscular atrophy, seen at times in general paralysis, to these cellular lesions.

While cellular lesions have been noted in a number of cases of polyneuritis, they do not always occur. In at least two cases reported in the literature they were absent; these are the case of Soukhanoff[36] and the one of Dejerine and Thomas.[37] In the latter very notable lesions of the cutaneous and muscular nerves were observed, but the spinal cells examined by the method of Nissl were normal. Dejerine and Thomas think that it is possible that the nerve cells had been altered, but had recovered, inasmuch as the neuritis had improved. They think also that chromatolysis of the cells, observed in intoxications and infections, is interesting cytologically, but has little real importance, and may not cause any symptoms.

The changes in the cells of the anterior horns which Ballet and Lebon have found in myelitis produced in the cords of rabbits by the injection of cultures of the pneumococcus and the staphylococcus (Ballet, l. c. 434) consist in destruction of the chromophilic elements, and no mention is made of the peripheral zone of degeneration in the cell seen in compression of the abdominal aorta. In Ballet and Lebon's experiments the roots and peripheral nerves were intact, or only slightly altered. The cells must have been primarily altered, and the changes were not unlike those observed after section of the nerve fibres.

Ballet and Dutil,[38] in a paper read at the recent congress in Moscow, stated that different poisons affect the cells differently, but that the early changes caused by compression of the abdominal aorta are much like the secondary cellular changes caused by cutting a peripheral nerve, and that, while the distinction of primary and secondary cellular changes is proper, under certain circumstances, it is impossible.

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[35] Berger: Monatsschrift f. Psychiatrie und Neurologie, vol. iii., No. 1.

[36] Soukhanoff: Archiv de Neurologie, 1896, vol. i., p. 177.

[37] Dejerine and Thomas: Comptes rendus de la Société de Biologie, 1897.

[38] Ballet and Dutil: Monatsschrift f. Psychiatrie und Neurologie, vol. ii., No. 5, p. 397.

It seems most probable that the nucleus is a very important part of the cell, and that on the normal condition of this the health of the entire neuron depends, but it is not unreasonable to believe that the axis cylinder is, to some extent, perhaps only a limited extent, independent of the cell body. It is very difficult to believe that the whole trophic function of an axis cylinder, extending, for example, from the lumbar region to the foot, can reside in a body so small as the nucleus. It has been thought that the medullary sheath is for the purposes of insulation and protection to the neuraxon, and that its interruption at the nodes of Ranvier is for the purpose of affording nutritious fluids an entrance to the axis cylinder. This seems to be a reasonable supposition.

The swelling of a few of the axis cylinders of the posterior roots in our case, as shown by the carmine stain, is interesting. The method of Marchi shows many black dots in both the anterior and the posterior roots. Changes in the posterior roots, after amputation, have been observed by a number of writers, and, therefore, we should not be surprised to observe this in polyneuritis. Fleming[39] has noticed very decided changes in the cells of the spinal ganglia after section of the sciatic nerve, and the degeneration of these cells was noticed at a much earlier period than that of the multipolar cells in the cord, beginning as early as the fourth day, and certainly by the seventh. Redlich, as well as Darkschewitsch (cited by

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[39] Fleming: The Edinburgh Medical Journal, New Series, vol. i., 1897.

Flatau), found degeneration of the posterior roots after amputation, indicating that the process had extended even beyond the spinal ganglia.

Flatau[40] was able to observe degeneration of the posterior roots after recent amputation in man when he employed the method of Marchi.

Lugaro[41] found that the cells of the spinal ganglia belonging to the sciatic nerve were much altered when this nerve in the dog was cut, but that no distinct changes in the ganglia were present when the posterior roots or the posterior columns of the cord were cut. Lugaro concluded that the cells of the spinal ganglion are altered in lesions of their peripheral branches, but not in lesions of their central. From these observations the central branch of the peripheral sensory neuron would seem to be a less vital portion of the cell than the peripheral branch.

Van Gehuchten[42] has observed the "reaction at distance" in the cells of the spinal ganglion after division of the peripheral nerve. Schaffer,[43] however, was unable to find any important change in these cells in tabes when he employed the method of Nissl, although he found the posterior roots greatly degenerated.

It would seem from these various statements that the "reaction at distance" does not occur in the spinal ganglion cell when its central process is cut or diseased, and does occur after lesion of the peripheral process.

Nissl stated that most of the cells in the nucleus of the seventh nerve recover after division of this nerve. Marinesco found that after he had divided the hypoglossal nerve in rabbits the nuclei in the cells of this nerve were only a little eccentric on the twenty-fourth day after the operation. It would seem, therefore, that the return of the nucleus to a central position within the cell is an early sign of cellular regeneration. In some cells he found the reparative process perinuclear, i. e., in the part which is first altered after division of a nerve fibre, but this was not seen in all the cells. Marinesco's[44] experiments cannot be used to determine the condition of the cells when peripheral reunion of the cut ends of the nerve fibre is prevented. Van Gehuchten[45] also has studied the cellular regeneration with similar results after experimental division of the nerve.

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[40] Flatau: Deutsche med. Wochenschrift, No. 18, 1897, p. 278.

[41] Lugaro (cited by Flatau): Fortschritte der Medicin, 1897, No. 15.

[42] Van Gehuchten: Journal de Neurologie et d'Hypnologie, 1897, p. 279.

[43] Schaffer: Neurologisches Centralblatt, No. 1, 1898.

We have the testimony of a number of writers that "reaction at distance" occurs in both sensory and motor neurons. In addition to the quotations already made, we may state that Sano[46] found chromatolysis of the cells of the column of Clarke after amputation of the lower limb, which he explained as "reaction at distance" from injury by meningitis to the nerve processes of these cells. He also found this reaction in the motor cells of the cord. Barker[47] gives the same explanation for the chromatolysis which he found in cells of Clarke's column in two cases of epidemic cerebrospinal meningitis. The direct cerebellar tract was injured. The changes in the motor cells he explains as the result of compression of their axis cylinders by the meningeal inflammation.

This, however, is not the only explanation which could be offered for the chromatolysis in the cells of Clarke's column in such cases. Marinesco[48] has found such changes in these cells in general paralysis and in tabes, diseases in which degeneration of the posterior roots is common, and he regarded these as secondary, and like those seen in polyneuritis. Van Gehuchten[49] also has found changes in the acoustic nucleus of the oblongata after division of the eighth nerve, i. e., in the cell body of the second neuron after injury of the peripheral neuron. The chromatolysis in the cells of the column of Clarke may, therefore, be the result of injury of posterior root fibres.

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[44] Marinesco: Comptes rendus de la Société de Biologie, 1896, p. 930.

[45] Van Gehuchten: Journal de Neurologie et d'Hypnologie, 1897, p. 279.

[46] Sano: Journal de Neurologie et d'Hypnologie, 1897.

[47] Barker: Brit. Med. Jour. 1897, vol. ii., p. 1,839.

[48] Marinesco: Revue Neurologique, 1896, p. 633.

Barker[50] acknowledges the possibility of the correctness of this explanation. He states that in his cases of epidemic cerebrospinal meningitis he found two distinct types of cellular change. In the first the disintegration of the Nissl bodies was especially marked in the dendrites and along the periphery of the cell, but these changes were slight, owing, he thinks, to the fact that cerebrospinal meningitis is an affection not associated with a severe toxæmia. In the second type the changes in the chromophilic elements were those described as "reaction at distance," i. e., they were chiefly in the centre of the cell and the nucleus was displaced. The first type Barker believes is the result of the direct action of the poison upon the cell body, and the second is due to injury of the axis cylinder.

He does not believe that the involvement of the posterior roots in his cases was sufficient to cut off enough of the sensory impulses to account for the changes found in almost every one of the cells of Clarke's column. This is a forcible argument, but we cannot forget the experiments of Babinski and Charrin, referred to above, which have shown that there may be a total loss of function of a nerve fibre without detectable lesions.

It is not extraordinary, therefore, that degeneration of the posterior roots should occur from polyneuritis. The involvement of the posterior roots and posterior columns in the disease has been noted by a number of observers, and

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[49] Van Gehuchten: Centralblatt f. Nervenheilkunde und Psychiatrie, Beiheft, October, 1897, p. 15.

[50] Barker: The Johns Hopkins Hospital Bulletin, February, 1898, p. 33.

Redlich[51] mentions such cases in his critical digest on diseases of the posterior columns of the cord. Pal and Redlich do not believe that the degeneration of the posterior roots is secondary to the neuritis. As Redlich expresses it, it is presumable that the poison acts on the entire sensory neuron at the same time. The possibility of this must, of course, be considered, but the observation of Flatau quoted above would indicate that the involvement of the posterior roots in polyneuritis may be secondary; for no other interpretation could well be given of his findings in these roots after amputation.

We do not always find the relations existing between disease of the motor cells, of the roots and of the peripheral nerves that we should expect. Thus, Gombault noted that the anterior roots were normal in a case of amyotrophic lateral sclerosis, although many of the motor cells had disappeared. Dreschfeld found marked lesions in the anterior cells of the cord while the intramuscular fibres were normal, and the nerves only slightly altered. Oppenheim reported similar conditions. V. Monakow, Zunker, Œller, Kronthal and Darkschewitsch (cited by Babinski[52]) have noted this want of correspondence in the intensity of the cellular changes and those of the nerves and roots, and recently Luce[53] has reported a case in which the cells of the anterior horns were much degenerated, and the anterior roots were only slightly affected. These cases would seem to indicate that the nerves enjoy an existence independent, to a certain extent, of the cell body.

Barbacci and Campacci[54] found that the nerve cells in the rabbit undergo postmortem changes They noticed that the chromophilic elements were paler and more indistinct than normal, and that they were changed into granules, especially about the nucleus, while the periphery of the cell was intact. In later stages vacuoles were found. Changes were seen also in the nucleus and nucleolus.

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[51] Redlich: Centralblatt f. allgemeine Pathologie und pathologische Anatomie, 1896.

[52] Babinski: Traité de Médecine, vol. vi., p. 650.

[53] Luce: Deutsche Zeitschrift f. Nervenheilkunde, vol. xii., No. 1.

[54] Barbacci and Campacci: Abstract in Neurologisches Centralblatt, 1897, p. 1,042.

Such findings must, of course, make us cautious in accepting all the cellular changes which are described as pathological, but they can hardly destroy the value of the work of many investigators. We, as others have done, have examined the spinal cord removed from persons some hours after death, who had not suffered from spinal or peripheral nerve lesions, and have not found any such changes as are present in our case of Landry's paralysis.

Held[55] has shown that the chromophilic elements do not exist in the living cell; that they are precipitated by the addition of fluids, and that they vary in form with the fluid used. He has likewise demonstrated that vacuoles in the protoplasm are postmortem changes, and may be produced by the addition of water.

These experiments throw light on the changes which occur within the cell under the influence of poisons. If the composition of the cellular protoplasm is chemically altered by toxic substances, the postmortem precipitation must be different from that in normal cells; or, if the function of the cell is destroyed by the cutting of its axis cylinder, the composition of the cellular protoplasm is most probably changed, and the precipitation must also be different. It matters little whether or not the Nissl elements are postmortem formations, as they always present the same appearance in normal cells; they afford, when altered, an index of the diseased condition of the cell.

Some quite recent experiments by Goldscheider and Flatau[56] have shown that great alteration of the chromophilic elements may exist without disturbance of function, and in a case of pneumonia Dejerine found the spinal cells swollen and without chromophilic elements, and the cellular processes altered. The patient had had no motor or sensory symptoms. This case Dejerine[67] brings forward in support of his views regarding the unimportance of chromatolysis.

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[55] Held: Archiv f. Anatomie und Entwickelungsgeschichte, 1895. p. 396.

[56] Goldscheider and Flatau: Fortschritte der Medicin, No. 7, 1897.

Ballet and Dutil[68] likewise have stated that the paralysis caused by compression of the abdominal aorta may disappear and motion be perfectly normal at a time when the spinal cells are still greatly altered.

Our conclusions, therefore, from a study of our case and of the literature, are:

1. That there is a form of ascending, flaccid paralysis, with little disturbance of sensation, with normal electrical reactions, and without involvement of the sphincters, and that this is of rapid course, usually terminating in death.
2. Other cases differ from this type by one or more atypical signs, and transitional forms occur which make the diagnosis between Landry's paralysis, polyneuritis and myelitis difficult.
3. It is possible that in some cases no lesions exist; but many of the reports of such cases date from a time when the methods of examination were very imperfect; or it may be that in these cases the lesions are in an early stage of development, the patient succumbing to toxæmia before demonstrable changes in the nervous system take place.
4. That Landry's paralysis may be due to myelitis alone.
5. In Landry's paralysis polyneuritis may be present, but changes in the cell bodies of the anterior horns will also usually be found in such cases by Nissl's stain, and it is sometimes difficult to say whether the cellular changes are primary or secondary.
6. It is probable, in some cases at least, that the entire peripheral motor neuron is attacked at the same time by the poison of the disease.

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[67] Dejerine: Comptes rendus de la Société de Biologie, 1897

[68] Ballet and Dutil: Monatsschrift f. Psychiatrie und Neurologie, vol. ii., No. 5.

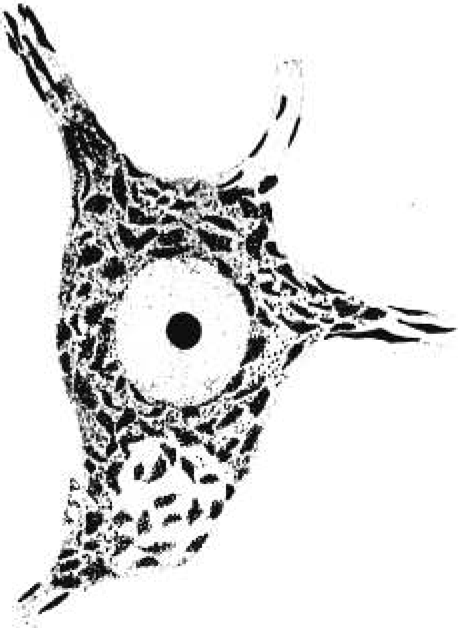

FIG. I.

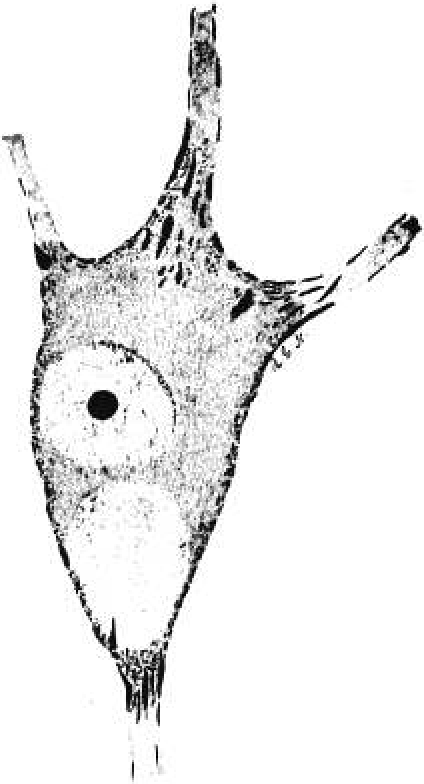

FIG. III.

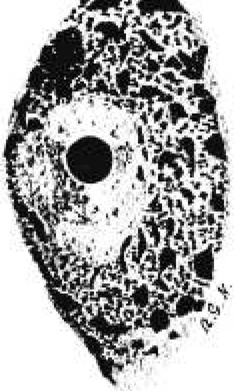

FIG. II.

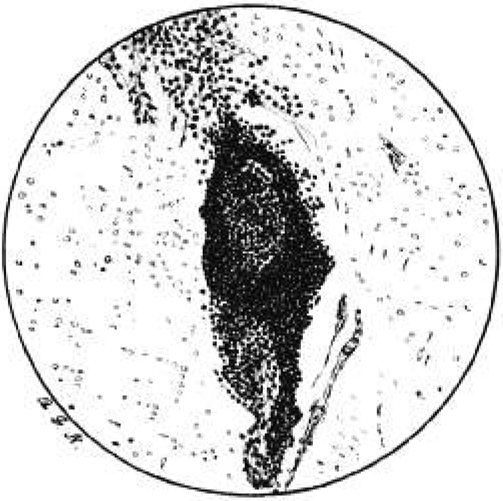

FIG. IV.

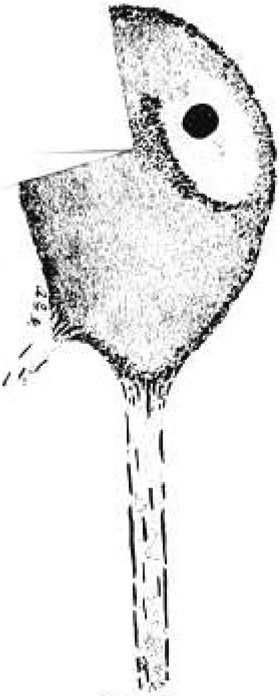

FIG. V.

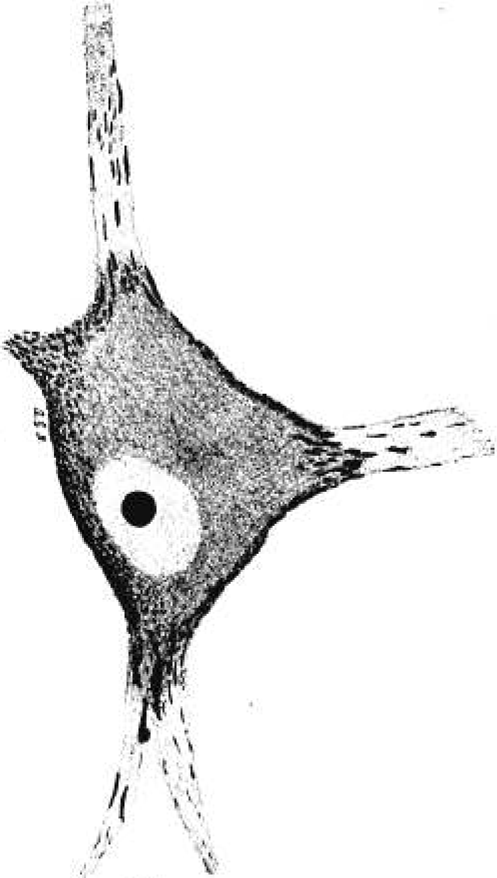

FIG. VI.

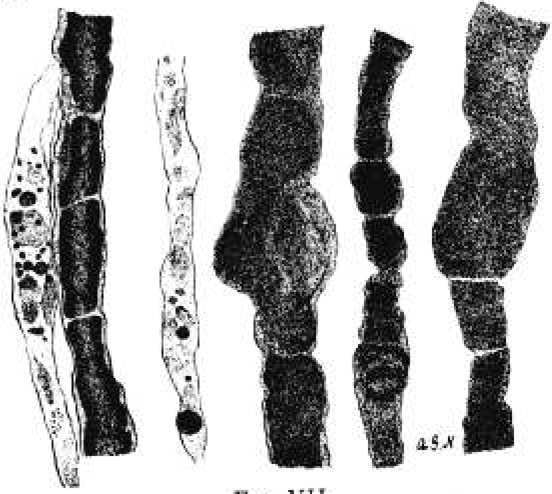

FIG. VII.

LEGENDS.

Figure 1: Normal cell from the hypoglossal nucleus.
Figure 2: Normal cell from Clarke's column.
Figure 3: Degenerated cell from the hypoglossal nucleus.
Figure 4: Round-cell infiltration in the oblongata.
Figures 5 and 6: Cells from the anterior horns of the spinal cord, showing central chromatolysis.
Figure 7: Nerve fibres from the external popliteal nerve, showing tumefaction and disintegration of the myelin.

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132. TABES UND MULTIPLE SKLEROSE IN IHREN BEZIEHUNGEN ZUM TRAUMA. (Tabes and Multiple Sclerosis in their Relation to Trauma). E. Mendel (Deutsche med. Wochenschr., p. 97, 1897).

Mendel comes to the conclusion, from his own experience, that trauma has not been clearly shown to be a cause of tabes. It often does cause a rapid development of pre-existing tabes, and in some cases tabetic patients, who until the occurrence of the trauma had been able to work, have become unable to earn their support after an accident. It is probable that the conditions connected with the trauma affect the disease, especially the long rest in bed. It is a well-known fact that tabetic patients have very imperfect use of their legs after a long confinement to bed. Hygienic conditions after such accidents also play a part in the development of tabetic symptoms. There is an important warning in this statement against prolonged rest cure with confinement to bed for tabetic patients.

There are certain cases of disseminated sclerosis which seem to result from trauma. Mendel reports four which he ascribes to this cause. It is hard to understand how trauma, which causes concussion of the entire central nervous system, can affect the posterior roots or posterior columns alone, as it must do to produce tabes. In a certain number of cases of multiple sclerosis, disturbance of the vascular system seems to have been the commencement of the disease, and it is not difficult to believe that trauma may cause changes in the blood pressure and other disturbances of circulation. The more imperfect vascular supply of the white matter may account for the greater frequency of the sclerotic patches in this part, as the conditions for recovery after a lesion are less favorable. There must, however, be a predisposition, as in many cases disseminated sclerosis does not develop after trauma. This predisposition probably consists of a less capability of resistance of the tissues to hyperæmia, and this predisposition may be congenital or acquired, as from some infectious disease.

SPILLER.